

United States Patent and Trademark Office

UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Virginia 22313-1450 www.uspto.gov

DATE MAILED: 02/28/2005

APPLICATION NO. FIRST NAMED INVENTOR CONFIRMATION NO. FILING DATE ATTORNEY DOCKET NO. 10/700,003 11/03/2003 Qiong Cheng CL1646USDIV EXAMINER 23906 7590 02/28/2005 E I DU PONT DE NEMOURS AND COMPANY PAK, YONG D LEGAL PATENT RECORDS CENTER ART UNIT PAPER NUMBER BARLEY MILL PLAZA 25/1128 4417 LANCASTER PIKE 1652 WILMINGTON, DE 19805

Please find below and/or attached an Office communication concerning this application or proceeding.

		Application No.	Applicant(s)
Office Action Summary		10/700,003	CHENG ET AL
		Examiner	Art Unit
		Yong D Pak	1652
The MAILING DATE of this communication appears on the cover sheet with the correspondence address Period for Reply			
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).			
Status			
1)⊠	Responsive to communication(s) filed on 03 No	ovember 2003.	
2a) <u></u> □	This action is FINAL . 2b)⊠ This	action is non-final.	
3)□	3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213.		
Disposition of Claims			
4)⊠ 5)□ 6)⊠ 7)□	 ✓ Claim(s) 23-29 and 36 is/are pending in the application. 4a) Of the above claim(s) is/are withdrawn from consideration. ☐ Claim(s) is/are allowed. ✓ Claim(s) 23-29 and 36 is/are rejected. ☐ Claim(s) is/are objected to. 		
Application Papers			
9) ☐ The specification is objected to by the Examiner. 10) ☑ The drawing(s) filed on <u>03 November 2003</u> is/are: a) ☑ accepted or b) ☐ objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d). 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.			
Priority under 35 U.S.C. § 119			
 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) All b) Some * c) None of: 1. Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No. 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received. 			
· · · · · ·			
Attachment(s)			
2) 🔲 Notic 3) 🔯 Inforr	e of References Cited (PTO-892) e of Draftsperson's Patent Drawing Review (PTO-948) nation Disclosure Statement(s) (PTO-1449 or PTO/SB/08) r No(s)/Mail Date 11/03/2003.	4) Interview Summary Paper No(s)/Mail Da 5) Notice of Informal Pa	

Application/Control Number: 10/700,003 Page 2

Art Unit: 1652

DETAILED ACTION

This application is a divisional of 09/934,903, now issued as U.S. Patent No. 6,660,507.

The preliminary amendment filed on November 3, 2003, canceling claims 1-22 and 30-35, amending claims 23-25 and adding claim 36, has been entered.

Claims 23-25, 26-29 and 36 are pending and are under consideration.

Information Disclosure Statement

Entries that are lined through on PTO form 1449 filed on November 3, 2003 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the Gen Bank references are not identified by an author, title or page numbers. They have been placed in the application file, but the information referred to therein has not been considered. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Specification

Examiner notes that applicants have not updated the relationship of the instant application to its parent application (09/934,903) that has matured into a U.S. patent (U.S. Patent No. 6,660,507). Examiner urges applicants to amend said information by providing the parent application number and its U.S. patent number in response to this Office action.

Biological Deposit

The statement filed on November 3, 2003, regarding the biological deposit of Methylomonas 16a ATCC PTA 2402 and its availability to the public, has been received.

Claim Objections

Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 25 ultimately depends from claim 23. Claim 23 is drawn to a method of using a polynucleotide encoding a pyrophosphate dependent phosphofructokinase of SEQ ID NO:4. However, claim 25 is drawn to a polynucleotide encoding any pyrophosphate dependent phosphofructokinase.

Art Unit: 1652

Claim 27 is objected to because of the following informalities: Claim 27 is objected for improper grammar. The claim recites the word "form" instead of "from" in line 2 which alters the overall meaning. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25 and claim 26 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 recites the term "gene". The metes and bounds of the phrase in the context of the above claim is not clear to the Examiner. A "gene" is generally understood in the art as comprising a coding sequence, introns, exons and regulatory sequences. A perusal of the specification did not provide the Examiner with a specific definition for the above term. Therefore, it is not clear whether the above term in said claims encompass the intronic and regulatory sequences or is limited to a cDNA. Examiner suggests replacing the above term with "polynucleotide".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 25-26 are drawn to a method for the production of isoprenoid compounds by using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase. The claims encompass a method for the production of isoprenoid compounds using a host cell comprising recombinants, variants and mutants of any pyrophosphate dependent phosphofructokinase. Therefore, the claim is drawn to a method of using a genus of polynucleotides encoding polypeptides having any structure. The specification only teaches a few species, polynucleotides encoding a pyrophosphate dependent phosphofructokinase of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18 and 24, all isolated from one source, Methylomonas 16a. These species isolated from one source is not enough and does not constitute a representative number of species to describe the whole genus there is no evidence on the record of the relationship between the structure of a polynucleotide encoding Methylomonas 16a pyrophosphate dependent phosphofructokinase of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14,

16, 18 and 24 and the structure of polynucleotides encoding any recombinants, variants and mutants of any pyrophosphate dependent phosphofructokinase. Therefore, the specification fails to describe the structure of the genus comprising polynucleotides encoding variants and mutants of any pyrophosphate dependent phosphofructokinase used for the production of isoprenoid compounds.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 25-26.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the production of carotenoids using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase of SEQ ID NO:4, does not reasonably provide enablement for a method for the production of any or all isoprenoid compounds using a host cell comprising a polynucleotide encoding mutants and variants of any or all pyrophosphate dependent phosphofructokinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Art Unit: 1652

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 25-26 are drawn to a method for the production of isoprenoid compounds by using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase. Therefore, the claim encompasses a method for the production of isoprenoid compounds using a host cell comprising a polynucleotide encoding recombinants, variants and mutants of any pyrophosphate dependent phosphofructokinase. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides encoding pyrophosphate dependent phosphofructokinase variants and mutants, broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited

to a method of producing isoprenoid compounds using a host cell comprising polynucleotides encoding a pyrophosphate dependent phosphofructokinase of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18 and 24, all isolated from one source, Methylomonas 16a. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides encoding variants and mutants of any pyrophosphate dependent phosphofructokinase. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass a method for the production of isoprenoid compounds using a host cell comprising a polynucleotide encoding all mutants and variants of any pyrophosphate

dependent phosphofructokinase, because the specification does not establish: (A) regions of the encoded protein structure which may be modified without affecting pyrophosphate dependent phosphofructokinase activity; (B) the general tolerance of pyrophosphate dependent phosphofructokinase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method for the production of isoprenoid compounds using a host cell comprising a polynucleotide encoding variants and mutants of any pyrophosphate dependent phosphofructokinase. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides encoding mutants and variants of any pyrophosphate dependent phosphofructokinase having the desired biological characteristics recited in the claim is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Art Unit: 1652

Claims 23-28 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the production of carotenoids using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase of SEQ ID NO:4, does not reasonably provide enablement for a method for the production of any or all isoprenoid compounds using a host cell comprising a polynucleotide encoding pyrophosphate dependent phosphofructokinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 23-28 and 36 are drawn to a method for the production of isoprenoid compounds by using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase. Therefore, the claims encompass a method for the production of any or all isoprenoid compounds using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase. The scope of the claims is not commensurate with the enablement provided by the disclosure with

regard to the extremely large number of isoprenoid compounds, broadly encompassed by the claims. The claims encompass compounds with widely varying structure and properties. However, in this case the disclosure is limited to a method for producing carotenoids with a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase. It would require undue experimentation of the skilled artisan to make any isoprenoid compounds. In view of the great breadth of the claims, amount of experimentation required to make the any or all isoprenoid compounds, the lack of guidance, working examples, and unpredictability of the art in predicting any or all isoprenoids compounds that can be produced with a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make the full scope of the isoprenoid compounds encompassed by the claims.

The specification does not support the broad scope of the claims which encompass a method for producing any or all isoprenoid compounds using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase, because the specification does not establish: (A) any or all isoprenoid compounds which can be produced using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase; (B) a rational and predictable scheme for making isoprenoid compound using a host cell comprising a polynucleotide encoding a pyrophosphate dependent

Art Unit: 1652

phosphofructokinase; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method for obtaining any or all isoprenoid compounds using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of carotenoid compounds that are produced by using a host cell comprising a polynucleotide encoding a pyrophosphate dependent phosphofructokinase recited in the claims are unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. (See rejection of claims 9-12 under 35 U.S.C. 112, 2nd)

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.

Art Unit: 1652

1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 27 is drawn to a method of producing isoprenoid compounds by transforming the plant cells recited in claim 27. The scope of the claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of plant host cells, broadly encompassed by the claims. The claims encompass plant host cells which are complex to transform. However, in this case the disclosure is limited to a method for transforming bacterial host cells with a polynucleotide encoding a pyrophosphate dependent phosphofructokinase. It would require undue experimentation of the skilled artisan to transform all the plant cells recited in the claim. In view of the great breadth of the claim, amount of experimentation required to transform all the recited plant cells, the lack of guidance, working examples, and unpredictability of the art in successfully transforming the recited plant cells with a polynucleotide encoding a pyrophosphate dependent phosphofructokinase and expressing a functional enzyme, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make the full scope of transforming the plant cells encompassed by the claim.

The specification does not support the broad scope of the claims which encompass a method for producing isoprenoid compounds by transforming all the recited plant cells with a polynucleotide encoding a pyrophosphate dependent phosphofructokinase, because the specification does not establish: (A) a method of successfully transforming the recited plant cells with a polynucleotide encoding a pyrophosphate dependent phosphofructokinase and expressing a functional enzyme; (B) a rational and predictable scheme for transforming all the recited plant cells with a polynucleotide encoding a pyrophosphate dependent phosphofructokinase; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method for obtaining isoprenoid compounds using all the recited plant cells transformed with a polynucleotide encoding a pyrophosphate dependent phosphofructokinase. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the recited plant cells expressing a functional enzyme encoded by a polynucleotide encoding a pyrophosphate dependent phosphofructokinase recited in the claim are unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Art Unit: 1652

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-29 and 36 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 7, 12, 13, 38-40 and 48-50 of copending Application No. 09/941,947 (which has been allowed and is in issue). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are claiming common subject matter, as follows: Claims 23-29 and 36 of the instant application and claims 1, 3, 7, 12, 13, 38-40 and 48-50 of the reference application are both directed to a method for the production of isoprenoid compounds comprising contacting host cell transformed with a polynucleotide encoding an enzyme in the isoprenoid biosynthetic pathway.

Carotenoids belong to the class of isoprenoid compounds. The enzyme of the reference application and the encoded pyrophosphate dependent phosphofructokinase of SEQ ID NO:4 of the instant invention are the same since a pyrophosphate dependent phosphofructokinase is involved in the isoprenoid biosynthetic pathway.

Page 16

Art Unit: 1652

Claims 23-29 and 36 of the instant application are drawn to a method for the production of isoprenoid compounds comprising contacting host cell transformed with a polynucleotide encoding a pyrophosphate dependent phosphofructokinase of SEQ ID NO:4. Claims 1, 3, 7, 12, 13, 38-40 and 48 of the reference application are drawn to a method for the production of carotenoid compounds comprising contacting host cell transformed with a polynucleotide encoding an enzyme in the carotenoid biosynthetic pathway. Claims 49-50 of the reference application are drawn to a method for the production of carotenoid compounds comprising contacting host cell transformed with a polynucleotide encoding a phosphofructokinase of SEQ ID NO:8 which is 100% identical to SEQ ID NO:4 of the instant invention (see Sequence Alignment – form PTO-892). Carotenoids belong to the class of isoprenoid compounds. A method for the production of isoprenoids with a host cell comprising a polynucleotide encoding SEQ ID NO:4 of the instant invention is a specific embodiment of the method described in the reference application. The specification of the reference application supports a method of using a host cell transformed with a polynucleotide encoding a phosphofructokinase of SEQ ID NO:4 (pages 8 and 11) that would anticipate the method of the instant invention. Claims 23-29 and 36 of the instant application cannot be considered patentably distinct over claims 1, 3, 7, 12, 13, 38-40 and 48-50 of the reference application when there is specifically recited embodiment that would anticipate claims 23-29 and 36 of the instant application.

Alternatively, claims 23-29 and 36 of the instant application cannot be considered patentably distinct over claims 1, 3, 7, 12, 13, 38-40 and 48-50 of the reference

application because it would have been obvious to one having ordinary skill in the art to modify claims 1, 3, 7, 12, 13, 38-40 and 48-50 of the reference application by selecting a specifically disclosed embodiment that supports those claimed, i.e. a method of producing isoprenoid compounds using a host cell comprising a polynucleotide encoding SEQ ID NO:4. One of ordinary skill in the art would have been motivated to do this because the embodiments claimed in the instant claims are disclosed as being a preferred embodiment within claims 1, 3, 7, 12, 13, 38-40 and 48-50 of the reference application. Therefore, the conflicting claims are not patentably distinct from each other.

This is a <u>provisional</u> obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak Patent Examiner 1652

Manjunath Rao Primary Examiner 1652 Page 17

Page 18

Art Unit: 1652